


FORM PTO 1590 (REV 3-93)		US DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY DOCKET NUMBER 2001_0572A
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. §371				U.S. APPLICATION NO. 09/831452 (if known, see 37 CFR 1.53) NEW
International Application No. PCT/JP99/06309		International Filing Date November 12, 1999		Priority Date Claimed November 12, 1998
Title of Invention PROTEIN AMSH AND cDNA THEREOF				
Applicant(s) For DO/EO/US Kazuo SUGAMURA and Nobuyuki TANAKA				
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:				
1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. §371. 2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. §371. 3. <input type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. §371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. §371(b) and PCT Articles 22 and 39(1). 4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date. 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. §371(c)(2)) a. <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau). b. <input checked="" type="checkbox"/> has been transmitted by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US) 6. <input checked="" type="checkbox"/> A translation of the International Application into English (35 U.S.C. §371(c)(2)). ATTACHMENT A 7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. §371(c)(3)). a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau). b. <input type="checkbox"/> have been transmitted by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19. 9. <input checked="" type="checkbox"/> An unexecuted oath or declaration of the inventor(s) (35 U.S.C. §371(c)(4)). ATTACHMENT B 10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. §371(c)(5)). Items 11. to 14. below concern other document(s) or information included: 11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. ATTACHMENT C 12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 13. <input checked="" type="checkbox"/> A FIRST preliminary amendment. ATTACHMENT D <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. 14. <input type="checkbox"/> Other items or information:				

THE COMMISSIONER IS AUTHORIZED
 TO CHARGE ANY DEFICIENCY IN THE
 FEE FOR THIS PAPER TO DEPOSIT
 ACCOUNT NO. 23-0975.

U.S. APPLICATION NO. 09/831452 NEW		INTERNATIONAL APPLICATION NO. PCT/JP99/06309		ATTORNEY'S DOCKET NO. 2001 0572A					
15. <input checked="" type="checkbox"/> The following fees are submitted BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)): Neither international preliminary examination fee nor international search fee paid to USPTO and International Search Report not prepared by the EPO or JPO \$1000.00 International Search Report has been prepared by the EPO or JPO \$ 860.00 International preliminary examination fee not paid at USPTO but international search paid to USPTO \$ 710.00 International preliminary examination fee paid to USPTO but claims did not satisfy provisions of PCT Article 33(1)-(4) \$ 690.00 International preliminary examination fee paid at USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) \$ 100.00 ENTER APPROPRIATE BASIC FEE AMOUNT =				<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 50%;">CALCULATIONS</th> <th style="width: 50%;">PTO USE ONLY</th> </tr> <tr> <td style="height: 100px; vertical-align: bottom;">\$860.00</td> <td></td> </tr> </table>		CALCULATIONS	PTO USE ONLY	\$860.00	
CALCULATIONS	PTO USE ONLY								
\$860.00									
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				\$					
Claims	Number Filed	Number Extra	Rate						
Total Claims	-20 =		X \$18.00	\$					
Independent Claims	- 3 =		X \$80.00	\$					
Multiple dependent claim(s) (if applicable)			+ \$270.00	\$					
TOTAL OF ABOVE CALCULATIONS =				\$860.00					
<input type="checkbox"/> Small Entity Status is hereby asserted. Above fees are reduced by 1/2.				\$					
SUBTOTAL =				\$860.00					
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				\$					
TOTAL NATIONAL FEE =				\$860.00					
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40 per property +				\$					
TOTAL FEES ENCLOSED =				\$860.00					
				Amount to be refunded	\$				
				Amount to be charged	\$				
a. <input checked="" type="checkbox"/> A check in the amount of \$860.00 to cover the above fees is enclosed. A duplicate copy of this form is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. 23-0975 in the amount of \$_____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23-0975.									
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.									
19. CORRESPONDENCE ADDRESS <div style="text-align: center;">  000513 PATENT TRADEMARK OFFICE </div>			By: <u>Warren M. Cheek, Jr.</u> Warren M. Cheek, Jr., Registration No. 33,367 WENDEROOTH, LIND & PONACK, L.L.P. 2033 "K" Street, N.W., Suite 800 Washington, D.C. 20006-1021 Phone: (202) 721-8200 Fax: (202) 721-8250 May 10, 2001						

[CHECK NO. nnn13]

[2001_0572A]



09831452 051001
JC16 Rec'd PCT/PTO 29 MAY 2002
Box 509

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of : Confirmation No. 4276
Kazuo SUGAMURA et al. : Docket No. 2001-0572A
Serial No. 09/831,452 : Group Art Unit Not Yet Assigned
Filed July 10, 2001 : Examiner Not Yet Assigned
PROTEIN AMSH AND cDNA THEREOF :

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents,
Washington, D.C. 20231

Sir:

Responsive to the Notice dated April 29, 2002, please amend the above-identified application as follows:

In the Sequence Listing:

Please replace the Sequence Listing of record with the attached substitute Sequence Listing.

REMARKS

The foregoing amendments are presented to place the application in compliance with the sequence rules under 37 CFR 1.821-1.825.

Applicants have submitted a Sequence Listing in both paper and computer readable form as required by 37 C.F.R. 1.821(c) and (e). Amendments directing its entry into the specification

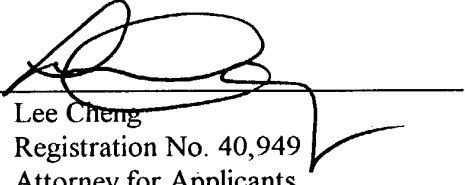
have also been incorporated herein. The content of the paper and computer readable copies are the same and no new matter has been added.

In view of the foregoing, it is believed that each requirement set forth in the Notice has been satisfied, and that the application is now in compliance with the sequence rules under 37 CFR 1.821-1.825. Accordingly, favorable examination on the merits is respectfully requested.

Respectfully submitted,

Kazuo SUGAMURA et al.

By: _____


Lee Cheng
Registration No. 40,949
Attorney for Applicants

LC/gtn
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
May 29, 2002



09/831,452, 05/01/01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of : **Confirmation No. 4276**
Kazuo SUGAMURA et al. : Docket No. 2001-0572A
Serial No. 09/831,452 : Group Art Unit Not Yet Assigned
Filed July 10, 2001 : Examiner Not Yet Assigned
PROTEIN AMSH AND cDNA THEREOF :

RESPONSE

Assistant Commissioner for Patents,
Washington, D.C. 20231

Sir:

Responsive to the Notice dated April 29, 2002, there is submitted herewith, in a separate Preliminary Amendment, a paper copy of a revised Sequence Listing for the above-identified application which has been prepared in accordance with the sequence rules under 37 CFR 1.821-1.825. The Sequence Listing contains the identical sequences appearing in the original application papers. Thus, no new matter has been added.

There is also submitted herewith a copy of the revised Sequence Listing in computer readable form as required by 37 CFR 1.821(e). The content of the paper and computer readable copies are the same.

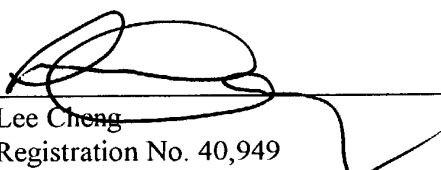
A copy of the Notice is also attached as required.

In view of the foregoing, it is believed that each requirement set forth in the Notice has been satisfied, and that the application is now in compliance with the sequence rules under 37 CFR 1.821-1.825. Accordingly, favorable examination on the merits is respectfully requested.

Respectfully submitted,

Kazuo SUGAMURA et al.

By: _____


Lee Cheng
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Telephone (202) 721-8200
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May 29, 2002

09/831452
JC08 Rec'd PCT/PTO 10 MAY 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :
Kazuo SUGAMURA et al. : Attn: BOX PCT
Serial No. NEW : Docket No. 2001_0572A
Filed May 10, 2001 :

PROTEIN AMSH AND cDNA THEREOF
[Corresponding to PCT/JP99/06309
Filed November 12, 1999]

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents,
Washington, DC 20231

Sir:

Prior to calculating the filing fee, please amend the above-identified application as follows:

IN THE SPECIFICATION

Page 1, immediately after the title, please insert:

This application is a 371 of PCT/JP99/06309 filed November 12, 1999.

IN THE CLAIMS

Please amend the claims as follows:

5. (Amended) A recombinant vector containing the hAMSH cDNA of claim 3.
11. (Amended) A recombinant vector containing the mAMSH cDNA of claim 9.

Please add the following new claims:

13. A recombinant vector containing the DNA fragment of claim 4.
14. A recombinant vector containing the DNA fragment of claim 10.

REMARKS

The specification has been amended to reflect the 371 status. In addition, the multiple dependencies of the claims have been removed to reduce the PTO filing fee.

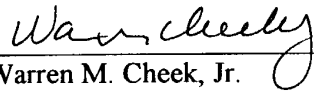
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned **"Version with markings to show changes made"**.

Favorable action on the merits is solicited.

Respectfully submitted,

Kazuo SUGAMURA et al.

By


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Telephone (202) 721-8200
Facsimile (202) 721-8250
May 10, 2001



SEQUENCE LISTING

<110> SUGAMURA, Kazuo
TANAKA, Nobuyuki

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DESCRIPTION

Protein AMSH and cDNA thereof

5 This application is a 371 of PCT/JP99/06309 filed November 12, 1999.

Technical Field

10 The present invention relates to human protein hAMSH and mouse protein mAMSH, and cDNAs encoding these proteins. More particularly, the present invention relates to novel human and mouse signal transduction molecules, AMSH, human and mouse genes encoding these proteins, cDNAs thereof, and antibodies against these proteins.

15

Background Art

20 A variety of cells having different functions should collaborate with each other for expression of higher biological functions such as hematopoietic, immunological and nervous systems. Communication among the cells is essential for their collaborations. Cytokines are known to be the proteins responsible for intercellular communication, and include interleukin (IL)-1 to 18, colony stimulation factors (CSFs), interferons (IFNs) and several chemokines.

25

30 Signals are generated by binding of the cytokines to specific receptors on the cell membrane, and survival, proliferation, differentiation and functional expression of the cells are controlled by signal transduction. Accordingly, dysfunction of cytokine-receptor signal transduction pathways result in collapse of the immunological and hematopoietic systems to cause severe infectious diseases, cancers and autoimmune diseases.

1. A human protein hAMSH having the amino acid sequence of SEQ ID No. 1.

5

2. A human gene encoding the human protein hAMSH of claim 1.

3. cDNA of the human gene of claim 2, which is hAMSH cDNA having the nucleotide sequence of SEQ ID no. 2.

10

4. A DNA fragment comprising a partial sequence in the nucleotide sequence of SEQ ID No. 2.

15

5. A recombinant vector containing the hAMSH cDNA of claim 4 or the DNA fragment of claim 4.

6. An antibody against the human protein hAMSH of claim 1.

20

7. A mouse protein mAMSH having the amino acid sequence of SEQ ID No. 3.

8. A mouse gene encoding the mouse protein mAMSH of claim 7.

25

9. cDNA of the mouse gene of claim 7, which is mAMSH cDNA having the nucleotide sequence of SEQ ID no. 4.

10. A DNA fragment comprising a partial sequence in the nucleotide sequence of SEQ ID No. 4.

30

11. A recombinant vector containing the mAMSH cDNA of claim 9, ~~or the~~
~~DNA fragment of claim 10.~~

DESCRIPTION

Protein AMSH and cDNA thereof

5

Technical Field

The present invention relates to human protein hAMSH and mouse
10 protein mAMSH, and cDNAs encoding these proteins. More particularly, the
present invention relates to novel human and mouse signal transduction
molecules, AMSH, human and mouse genes encoding these proteins, cDNAs
thereof, and antibodies against these proteins.

15

Background Art

A variety of cells having different functions should collaborate with
each other for expression of higher biological functions such as
20 hematopoietic, immunological and nervous systems. Communication
among the cells is essential for their collaborations. Cytokines are known to
be the proteins responsible for intercellular communication, and include
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and several chemokines.

25

Signals are generated by binding of the cytokines to specific
receptors on the cell membrane, and survival, proliferation, differentiation
and functional expression of the cells are controlled by signal transduction.
Accordingly, dysfunction of cytokine-receptor signal transduction pathways
30 result in collapse of the immunological and hematopoietic systems to cause
severe infectious diseases, cancers and autoimmune diseases.

For the reasons described above, it is quite important to elucidate the intracellular signal transduction pathways mediated by the cytokine/cytokine receptor system. This is important, in order to appreciate the basic phenomena such as proliferation and differentiation of the cells, pathogenesis, diagnosis and therapeutic intervention of various diseases at the molecular levels.

The inventors of the present invention have isolated the genes of "common γ -chain" commonly included in a plurality of the cytokine receptors, and have made a great contribution in elucidating the structure and function of the cytokine receptors. Of particular elucidation is that the γ -chain is an essential subunit for functional expression of IL-2, IL-4, IL-7 and IL-9, and abnormality in the γ -chain causes impairment of early development of T-cells via dysfunction of IL-7 (Science, 262:1874-1877, 1993; Int. Immunol., 6:1451-1454, 1994; Science, 263:1453-1454, 1994; Eur. J. Immunol., 25:3001-3005, 1995).

Recently, the inventors of the present invention have identified "STAMs" as novel signal molecules concerning signal transduction in the proliferating cells by the cytokines, and found that these STAMs are present downstream of the IL-2/GM-CSF receptor and directly associate with JAK3/2. The inventors also found that STAMs play an important role in expression of c-myc and signal transduction for DNA synthesis (Immunity, 6:449-457, 1997).

While several important mechanisms of the intracellular signal transduction pathway by binding of the cytokines to the receptors have been made clear, additional novel molecules should be identified for elucidating the overall structure and function of the intracellular signal transduction pathway, because plural molecules are thought to be continuously and synergetically involved in the signal transduction pathway and to manifest final functional

Best Mode for Carrying Out the Invention

5 The procedure for obtaining a human protein hAMSH and cDNA thereof, as well as the procedure for identifying the function of the protein will be described hereinafter.

10 The human protein hAMSH cDNA according to the present invention is a human gene's cDNA isolated by screening a human cDNA library by Far-Western method using a chimera gene of SH3 domain of STAM gene and glutathione-S-transferase (GST). This cDNA has a nucleotide sequence comprising 1910 base pairs shown in SEQ ID No. 2, and encodes the protein hAMSH having the amino acid sequence of SEQ ID No. 1.

15 While estimated a nucleus transfer signal and a JAB1-like structure are observed in the molecule of the protein hAMSH, this protein is confirmed to be a novel molecule since corresponding molecules are not found in the protein data base.

20 The facts that this protein hAMSH is a novel molecule involved in signal transduction for cell proliferation by association with STAM, downstream of the cytokine receptor, is confirmed as follows:

- 25 (1) AMSH-dc2 in which half of the C-terminal region of hAMSH has been deleted, suppresses signal transduction for DNA synthesis after stimulating with IL-2 and GM-CSF; and
- (2) The AMSH-dc2 mutant suppresses c-myc inducing signal transduction after stimulating with IL-2 and GM-CSF.

30 The cDNA of the mouse protein mAMSH according to the present invention is a mouse gene's cDNA isolated by screening a mouse cDNA

library using the hAMSH cDNA as a probe. This cDNA has the nucleotide sequence comprising 1384 base pairs shown in SEQ ID No. 4, and encodes the protein mAMSH having the amino acid sequence of SEQ ID No. 3.

5 The proteins hAMSH and mAMSH according to the present invention may be obtained by conventional methods such as isolating from human or mouse organs or from cell lines, preparing the peptides by a chemical synthesis based on the amino acid sequence provided by the present invention, or by a recombinant DNA techniques using the cDNA
10 fragments provided by the present invention. For example, in order to obtain the protein hAMSH by the recombinant DNA technique, RNA is prepared by in vitro transcription from the vectors comprising cDNA fragment having the nucleotide sequence of SEQ ID No. 2, and the protein may be expressed through in vitro translation using the RNA as a template.
15 The protein encoded by the cDNA may be also expressed in large scale in E. coli, Bacillus subtilis, yeast, animal cells and plant cells by recombining an expression vector with the translation region of cDNA by known methods in the art.

20 When the protein according to the present invention is produced by expression of DNA by in vitro translation, the cDNA or its translation region is recombined into a vector having a RNA polymerase promoter, and the recombinant cDNA is added in an in vitro translation system such as a rabbit dialyzate or wheat germ extract containing a RNA polymerase for the
25 promoter. Examples of the RNA polymerase promoter include T6, T3 and SP6. Examples of the vector containing these RNA polymerase promoter include pKA1, pCDM8, pT3/7 18, pT7/3 19 and pBlueprint II.

30 For large scale production of the protein encoded in cDNA in microorganisms such as E. coli, an expression vector is constructed by inserting the cDNA according to the present invention or its translation region into an expression vector comprising an origin suitable for

microorganisms, a promoter, a ribosome binding site, cDNA cloning sites and terminator, followed by cultivation of the transformant cell obtained after translocation of the host cell with the expression vector. A protein containing an arbitrary region can be obtained by allowing the expression
5 vector to express by adding an initiation codon and a stop codon before and after the arbitrary translation region. Otherwise, a desired protein portion can be selectively obtained by allowing the protein to express as a fusion protein with other protein, followed by cleaving this fusion protein with an appropriate protease. Examples of the expression vector for use in E. coli
10 include pUC, pBluescript II, pET expression system and pGEX expression system.

For producing the protein according to the present invention in eukaryotic cell such as animal cells, the cDNA or the translation region
15 thereof is inserted into an expression vector for the eukaryotic cell comprising a promoter, splicing region and poly (A) addition site to introduce the recombinant vector into the eukaryotic cell. Examples of the expression vector include pKA1, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS and pYES2. While cultured cells of a mammal such as
20 monkey kidney cells COS7 and Chinese hamster ovary cells CHO, budding yeast, dividing yeast, silkworm cells and African clawed frog egg cells are usually used as the eukaryotic cells, any eukaryotic cells may be used so long as they are able to express MIST. The expression vector can be introduced into the eukaryotic cell by a conventional method such as an
25 electroporation method, a calcium phosphate method, a liposome method and a DEAE dextran method.

Separation procedures known in the art may be combined for isolating and purifying the desired protein from the culture after expressing
30 the protein in microorganisms or eukaryotic cells. The separation and purifying methods include, for example, treatment with a denaturation reagent such as urea or with a surface active agent, ultrasonic treatment,

plural amino acids, and/or substitution with other amino acids caused by the alteration of cDNAs may be also included within the scope of the present invention, provided that the protein comprises protein activity of the protein having the amino acid sequence of SEQ ID No. 1 or 3.

5

The DNA fragments (10 bp or more) comprising any partial nucleotide sequence of SEQ ID No. 2 or 4 are also included in the DNA fragment of the present invention. DNA fragments comprising sense strand and antisense strand may be categorized into the DNA fragment of the present invention. The DNA fragments can be used as a probe for gene diagnosis.

10

Antibodies against the proteins of the present invention may be obtained as polyclonal antibodies or monoclonal antibodies by conventional methods using the proteins themselves or partial peptides thereof as antigens.

15

Example

20

A part of the hAMSH cDNA (the 383-550th in SEQ ID No. 2: corresponds to the amino acids 125-180th in SEQ ID No. 1) was amplified by PCR and was inserted into the GST fusion protein expression vector. This vector was introduced into E coli for transformation, and this transformant was stimulated with IPTG to induce expression of the GST fusion protein. The induced fusion protein was purified by affinity chromatography using a glutathione column, thereby obtaining the GST fusion protein. An antiserum was obtained by immunizing a rabbit with this GST fusion protein as an antigen.

25

30

Industrial Applicability

As hitherto described in detail, the present invention provides novel signal transduction molecules related to the cytokine based signal transduction pathway, and gene engineering materials. These molecules and gene engineering materials are useful for developing diagnostic and therapeutic methods as well as pharmaceuticals for human diseases due to dysfunction of the cytokine based signal transduction pathway such as severe infectious diseases, cancers and autoimmune diseases.

CLAIMS

1. A human protein hAMSH having the amino acid sequence of SEQ ID
No. 1.

5

2. A human gene encoding the human protein hAMSH of claim 1.

3. cDNA of the human gene of claim 2, which is hAMSH cDNA having
the nucleotide sequence of SEQ ID no. 2.

10

4. A DNA fragment comprising a partial sequence in the nucleotide
sequence of SEQ ID No. 2.

5. A recombinant vector containing the hAMSH cDNA of claim 4 or the
DNA fragment of claim 4.

15

6. An antibody against the human protein hAMSH of claim 1.

7. A mouse protein mAMSH having the amino acid sequence of SEQ ID
No. 3.

20

8. A mouse gene encoding the mouse protein mAMSH of claim 7.

9. cDNA of the mouse gene of claim 7, which is mAMSH cDNA having
the nucleotide sequence of SEQ ID no. 4.

25

10. A DNA fragment comprising a partial sequence in the nucleotide
sequence of SEQ ID No. 4.

11. A recombinant vector containing the mAMSH cDNA of claim 9 or the
DNA fragment of claim 10.

30

12. An antibody against the mouse protein mAMSH of claim 7.

ABSTRACT

This application provides a human protein AMSH having the amino acid sequence of SE ID No. 1 which is a novel signal transduction molecule
5 interacting with the SH3 domain of cytokine based signal transduction molecule STAM; a gene encoding the above AMSH; a cDNA having the nucleotide sequence of SEQ ID No. 2; and antibody against AMSH.



091331452 061001

Rev. 3-21-01

Effective March 1998

DECLARATION AND POWER OF ATTORNEY FOR U.S. PATENT APPLICATION

(X) Original () Supplemental () Substitute (X) PCT () DESIGN

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that I verily believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Title: PROTEIN AMSH AND cDNA THEREOF

of which is described and claimed in:

() the attached specification, or

(X) the specification in application Serial No. _____, filed May 10, 2001, and with amendments through _____, or(X) the specification in International Application No. PCT/JP99/06309, filed November 12, 1999, and as amended on _____ (if applicable).

I hereby state that I have reviewed and understand the content of the above-identified specification, including the claims, as amended by any amendment(s) referred to above.

I acknowledge my duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim priority benefits under Title 35, United States Code, §119 (and §172 if this application is for a Design) of any application(s) for patent or inventor's certificate listed below and have also identified below any application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:


COUNTRY	APPLICATION NO.	DATE OF FILING	PRIORITY CLAIMED
Japan	1998-322674	November 12, 1998	Yes

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION SERIAL NO.	U.S. FILING DATE	STATUS: PATENTED, PENDING, ABANDONED

And I hereby appoint Michael R. Davis, Reg. No. 25,134; Matthew M. Jacob, Reg. No. 25,154; Warren M. Check, Jr., Reg. No. 33,367; Nils Pedersen, Reg. No. 33,145; Charles R. Watts, Reg. No. 33,142; and Michael S. Huppert, Reg. No. 40,268, who together constitute the firm of WENDEROTH, LIND & PONACK, L.L.P., as well as any other attorneys and agents associated with Customer No. 000513, to prosecute this application and to transact all business in the U.S. Patent and Trademark Office connected therewith.

I hereby authorize the U.S. attorneys and agents named herein to accept and follow instructions from NISHIZAWA & ASSOCIATES as to any action to be taken in the U.S. Patent and Trademark Office regarding this application without direct communication between the U.S. attorneys and myself. In the event of a change in the persons from whom instructions may be taken, the U.S. attorneys named herein will be so notified by me.

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--	---

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	Residence & Citizenship	CITY <u>Miyagi</u>	STATE OR COUNTRY Japan	COUNTRY OF CITIZENSHIP <u>JPY</u> Japan
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	Residence & Citizenship	CITY	STATE OR COUNTRY	COUNTRY OF CITIZENSHIP
	Post Office Address	ADDRESS	CITY	STATE OR COUNTRY ZIP CODE
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	Residence & Citizenship	CITY	STATE OR COUNTRY	COUNTRY OF CITIZENSHIP
	Post Office Address	ADDRESS	CITY	STATE OR COUNTRY ZIP CODE
	Full Name of Fifth Inventor	FAMILY NAME	FIRST GIVEN NAME	SECOND GIVEN NAME
	Residence & Citizenship	CITY	STATE OR COUNTRY	COUNTRY OF CITIZENSHIP
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SEQUENCE LISTING

<110> Japan Science and Technology Corporation

<120> Protein AMSH and cDNA thereof

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```

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SECRET

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Residence & Citizenship	CITY	STATE OR COUNTRY	COUNTRY OF CITIZENSHIP
Post Office Address	ADDRESS	CITY	STATE OR COUNTRY ZIP CODE

I further declare that all statements made herein of my own knowledge are true, and that all statements on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

1st Inventor	<u>Kazuo SUGAMURA</u>	Date	<u>June 22, 2001</u>
2nd Inventor	<u>Nobuyuki TANAKA</u>	Date	<u>June 22, 2001</u>
3rd Inventor		Date	
4th Inventor		Date	
5th Inventor		Date	
6th Inventor		Date	

The above application may be more particularly identified as follows:

U.S. Application Serial No. _____ Filing Date May 10, 2001

Applicant Reference Number 99-F-054PCT-US/YS Atty Docket No. 2001 0572A

Title of Invention PROTEIN AMSH AND cDNA THEREOF